December 20, 2002

Kenneth P. Morgan
Manager, Technical Support Services
Merisol USA LLC
1914 Haden Road
Houston, Texas 77015-6498

Dear Mr. Morgan:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Ethylphenols Category posted on the ChemRTK HPV Challenge Program Web site on August 16, 2002. I commend the Merisol USA LLC for its commitment to the HPV Challenge Program.

EPA also must bring to your attention the fact that the acute toxicity test which you have proposed is specifically not recommended for use in the HPV Challenge Program (65 FR 81695) where the recommended guideline is OECD TG 425 (the "Up and Down Method"). In addition, the Organization for Economic Cooperation and Development (OECD) has made the decision to remove OECD TG 401, and test data using the guideline generated after December 20, 2002 need not be accepted by other OECD countries under Mutual Acceptance of Data. Note, also, that EPA encourages Challenge sponsors that have proposed acute toxicity testing to use an in vitro dose range-finding protocol to set the starting dose for the Up and Down test. Information on this protocol is available at http://www.epa.gov/chemrtk/toxprtcl.htm. Finally, EPA recommends an in vitro chromosomal aberration study instead of the in vivo micronucleus (OECD 474) proposed.

With the successful completion of the testing needed to address the category proposal, EPA will consider this as meeting a sponsorship commitment.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Merisol advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief

of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the “Contact Us” link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
W. Penberthy
A. Abramson
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission: Ethylphenols Category

SUMMARY OF EPA COMMENTS

The sponsor, Merisol USA LLC, submitted a test plan and robust summaries to EPA for the mixed ethylphenols category dated July 29, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on August 16, 2002. The category consists of 2-ethylphenol (o-ethylphenol, CAS No. 90-00-6); 3-ethylphenol (m-ethylphenol, CAS No. 620-17-7); and 4-ethylphenol (p-ethylphenol, CAS No. 123-07-9).

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. Given the close structural similarity of these isomers, the similar physicochemical properties, and the evidence demonstrating similar toxicities of members of an analogous series of methylphenol (cresol) isomers, it is reasonable to expect that the ethylphenol isomers will have toxicities similar to each other.

2. Physicochemical Properties and Environmental Fate. The submitted physicochemical data on three individual isomers are adequate for the purposes of the HPV Challenge Program. EPA believes that hydrolysis testing is not necessary. All new and existing data need to be presented in robust summary format.

3. Health Effects. EPA agrees with the submitter's test plan for addressing all health effects endpoints using the ethylphenol mixture but recommends testing a commercial ethylphenols mixture that either (a) is sold in the highest production volume, or (b) has the highest percentage of ethylphenol isomers.

4. Ecological Effects. EPA agrees with the submitter's test plan for addressing the ecological effects endpoints using the equimolar mixture. EPA notes that there is a published fish study for 4-ethylphenol (Geiger, 1986) not cited in the Test Plan, and in addition existing xylenols data could be used as supporting data for ethylphenols.

EPA requests that the submitter advise the Agency within 60 days of any modifications to this submission.

EPA COMMENTS ON THE ETHYLPHENOLS CHALLENGE SUBMISSION

General

This submission is similar to the Xylenols Category submission from the same sponsor. In reviewing both submissions, it appears that most of the submitter's commercial products are mixtures of xylenols, phenols, cresols, and ethylphenols. According to the Merisol Web site (www.merisol.com), the following xylenol products are available for sale: 2,4/2,5 xylenol mixture; "mixed xylenols and ethylphenols"; high purity xylenols (pure 3,4-isomer listed as what is currently available); and "blended cresylic acid products" (what appears to be the starting Merisol fraction used to develop the cresols, xylenols, and ethylphenols).

Table 1 in the test plan states that only 57.1% of the Merisol products contain all three ethylphenol isomers, but provides no information on the percentage composition range for xylenols, phenols, cresols, and ethylphenols in those products. The submitter needs to provide specific information on the percentages of the ethylphenol isomers in typical commercial products, with a description of the rest of the product composition.

Category Definition

The submitter has proposed a category of mixtures of three ethylphenol isomers: 2-ethylphenol; 3-ethylphenol; and 4-ethylphenol. Binary mixtures of the ethylphenol isomers constitute 42.3% of the blends and ternary mixtures compose 57.1% of the blends. The definition lacks specific information on composition (see previous section).

Category Justification

EPA agrees with the submitter's category justification. The justification is based on the close structural relationship of the ethylphenol isomers, and their similar physicochemical, and anticipated similar environmental and toxicological properties. The submitter has provided data on an analogous series of cresol isomers, which according to the submitter, demonstrate their close structural similarity, their similar physicochemical properties, and their similar toxicities. The submitter further states that it is reasonable to expect that the ethylphenol isomers will also have toxicities similar to each other. The submitter states that the toxicological properties of the ethylphenol mixtures will not significantly vary with the proportion of the ethylphenol isomers in the mixtures. However, for health effects, EPA prefers that the commercial substance be tested rather than a equimolar mixture.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

The submitted physicochemical data on three individual isomers are adequate for the purposes of the HPV Challenge Program.

The submitter needs to check the melting point values for p-ethylphenol and m-ethylphenol reported in Table 3 of the test plan. EPA found in EPIWIN and the CRC manual melting point values of 45 and 47 °C for p-ethylphenol (the submitter reported -4 °C), and -4 °C for m-ethylphenol (the submitter reported 46 °C).

Environmental Fate (photodegradation, biodegradation, fugacity, stability in water).

EPA agrees with the submitter's test plan for addressing environmental fate endpoints using the equimolar mixture. However, EPA believes that hydrolysis testing is not appropriate for these substances.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

The submitter acknowledged that available ethylphenol data may not be reliable and will

not be used for the purposes of the HPV Challenge Program. Because ethylphenols exist predominantly as mixtures in commerce, the submitter has proposed testing an equimolar mixture of the three ethylphenols to assess the potential hazards of exposure to ethylphenol-containing substances. The results of this testing would be applicable to all mixtures of ethylphenols and to each of the three individual isomers. Testing would include acute mammalian toxicity, a combined repeated-dose/reproductive/developmental toxicity screen, and genetic toxicity (assays for bacterial mutagenicity and mammalian erythrocyte micronuclei) and would be done according to OECD guidelines. EPA recommends that the submitter consider testing a commercial ethylphenols mixture that either (a) is sold in the highest production volume, or (b) has the highest percentage of ethylphenol isomers.

In Attachment I, a table titled "Cresols Isomer Mammalian Toxicity Comparison," it is difficult to compare the reproductive and developmental toxicity data for the three separate cresol isomers because presented dose levels were not clearly identified as NOAELs, no LOAELS were reported, and identified adverse effects were not associated with specific dose levels. Furthermore, robust summaries were not submitted for the two-generation reproductive toxicity study of m-cresol. More clearly identified NOAELs and LOAELS (with associated effects) would enhance the interpretation of the results presented in this table. A similarly-designed table should be prepared for acute and repeated-dose oral toxicity as well.

Ecological Effects (fish, invertebrates, and algae).

EPA agrees with the submitter's test plan for addressing all ecological effects endpoints using the equimolar mixture.

Specific Comments on the Robust Summaries

None.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modification to its submission.

References

Geiger, D.L., Poirier, S.H., Brooke, L.T., and Call, D.J. 1986. "Acute Toxicities of Organic Chemicals to Fathead Minnows (*Pimephales Promelas*)" Volume III, Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, US Environmental Protection Agency Cooperative Agreements, Superior, Wisconsin, USA.